



DAVINCI
MEDICAL
ACADEMY

SUBJECTS IN NUTSHELL FOR EFFECTIVE REVISION



PHYSIOLOGY IN NUTSHELL

HEAD OFFICE:

No.291/139, 3rd Floor, Thambu Chetty Street, Parry's, Chennai - 600 001.
Above; KHM Medical Center, Near; DCB Bank, Opp; Tata Docomo Showroom

Mobile: +91 9962850383 +91 9884329457

ELITE TEAM OF FACULTY



SOME OF OUR FMGE TOPPERS





DMA'S CORNER OF WISDOM

DEAD SPACE:

- **Anatomical** - Volume of air occupying the conducting zone (not participating in gaseous exchange). (150 ml), measured by **Bohr's method**.
-roughly **equal to body weight in pounds or twice the body wt. in kgs.**
 - **Physiological** dead space- volume of gas not equilibrating with blood, "WASTED VENTILATION", measured by **Fowler's method**.
 - **Under normal conditions, both are equal.**
- **Spirometer** measures all volumes & capacities **except RV, FRC and TLC**.
- Methods to measure RV & FRC:
 - ✓ Helium dilution technique
 - ✓ Plethysmography
 - ✓ Nitrogen washout method

SURFACTANT

- Produced by type-II alveolar cells
- Starts at 28 weeks of gestation & peaks at 35 weeks
- Composition: dipalmitoyl phosphatidyl choline (62%), neutral lipids (10%)
- Functions: - **reduces alveolar surface tension**
- **Prevent alveolar collapse**
- **Prevents pulmonary edema**
- Deficient conditions: **occlusion of main bronchus/pulmonary artery, smoking, long term inhalation of 100% oxygen**
- Deficiency causes: **IRDS/ Hyaline membrane disease, patchy atelectasis, pulmonary alveolar proteinosis.**

TRANSPORT OF GASES

- Amount of O₂ that enters the body- 250ml/min
- Amount of CO₂ excreted by the lungs-200ml/min (288L/day)
- So, respiratory quotient at rest = $200/250 = 0.8$

OXYGEN TRANSPORT:

- Mostly carried by attaching to hemoglobin
 - 1 gram of Hb combines with 1.34ml of O₂.
 - If the Hb is 15g%, then the maximal amount of O₂ per 100ml will be: $1.34(\text{Hb}) = 1.34(15) = 20\text{ml}$
- **Bohr's effect:** the presence of CO₂ decreases the affinity of Hb for O₂. It enhances further release of O₂ to the **tissues**.
- **Note: 1 liter of plasma combines with 3ml of O₂.** Basal O₂ requirement is 250 ml/min
- Hence in the absence of Hb, about 84 liters of plasma will be needed to meet the basal
 - Oxygen demand (250ml/min), as $250\text{ml}/3 = 84$.

CARBON DIOXIDE TRANSPORT:

- Mostly transported as bicarbonate: HCO₃ (70%)> Carbamino compounds (23%)>dissolved (7%)

Carbon dioxide forms	Arterial blood	Venous blood
Bicarbonate	✓ 45 ml	✓ 47 ml
Carbamino compounds	✓ 2.5 ml	✓ 3.5 ml
Dissolved form	✓ 2.5 ml	✓ 3 ml

- **Haldane's (Douglas/Christian) effect:**
- binding of O₂ with Hb displaces CO₂ from the blood in the **lungs**.

DMA'S CORNER OF WISDOM

○ **Chloride shift/ Hamburger phenomenon:**

- movement of HCO_3^- ions from the RBCs to the plasma result in inward flux of Cl^- ions to maintain the electrical equilibrium. It is mediated by band-3 membrane protein.

○ **The major buffer of CO_2 in the blood is Hb.**

○ **Hematocrit of venous blood is 3% higher than arterial blood.**

○ **Venous blood pH < Arterial blood pH.**

O₂ DISSOCIATION CURVE (ODC)

○ Graphical representation between PO_2 & percentage saturation of Hb

○ Normal is S-shaped/sigmoid shaped

○ **Factors shifting the ODC:**

Shift to the Right (Release/tissues)	Shift to the Left (Lungs/binding)
• Increased PCO_2 • Increased temperature • Increased 2,3-DPG as in Growth hormone, Exercise, Hypoxia, High altitude, Anemia • Acidosis (decreased pH) • Sick cell anemia • Adult Hb	• Decreased PCO_2 • Decreased temperature • Decreased 2,3-DPG as in • Alkalosis (increased pH) • Fetal Hb • Stored blood

MYOGLOBIN:

- ODC is a hyperbola.
- One molecule of Mb binds with only 1 molecule of O_2 [Hb which binds to 4 molecules]
- Does not show Bohr's effect

○ **NEUROGLOBIN: oxygen sensor in the brain & facilitates oxygen transport.**

GASEOUS EXCHANGE

OXYGEN EXCHANGE		CARBON DIOXIDE EXCHANGE	
FROM ATMOSPHERE TO ALVEOLI	○ PO_2 in the atmosphere- 159mmHg ○ PO_2 in the alveoli- 104mmHg. ○ Due to the pressure gradient, O_2 enters the alveoli.	FROM TISSUE TO THE BLOOD	• PCO_2 in the tissues- 46mmHg. • PCO_2 in the artery- 40mmHg. • Due to the pressure gradient, CO_2 enters the blood at the rate of 4 ml/100ml of blood
FROM ALVEOLI TO BLOOD	○ PO_2 in the alveoli- 104mmHg ○ PO_2 in the pulmonary artery- 64mmHg. ○ Due to the pressure gradient, O_2 enters the pulmonary artery. ○ The content of O_2 in the venous blood(pulmonary artery)=14ml% ○ The content of O_2 in arterial blood(pulmonary vein)=19ml% ○ Hence, the diffusion of O_2 from alveoli to blood is 5ml/100ml of blood.	FROM BLOOD TO ALVEOLI	• PCO_2 in the blood- 45 mmHg. • PCO_2 in alveoli- 40 mmHg. • Due to the pressure gradient, CO_2 enters the alveoli at the rate of 4 ml/100ml of blood
FROM BLOOD TO THE TISSUE	○ PO_2 in the systemic artery- 95 mmHg ○ PO_2 in the tissues- 40mmHg. ○ Due to the pressure gradient, O_2 enters the tissues. ○ The content of O_2 in arterial blood=19ml%	FROM ALVEOLI TO ATMOSPHERE	• In the atmosphere, PCO_2 is very insignificant, so CO_2 leaves the alveoli easily.

DMA: 291/139, 3rd floor, Thambu Chetty ST, Parrys, Chennai -01

Phone number: 044-42009468 Mail us: studyatdma@gmail.com

Web: www.dma-study.com & www.jzmustudy.com

DMA'S CORNER OF WISDOM

S	- The content of O₂ in the venous blood=14ml% - Hence, the diffusion of O₂ from to tissues is 5ml/100ml of blood.	HERE	
---	--	------	--

- Thus, the whole blood is an ideal vehicle for gaseous transport than plasma/Hb

COMPARISON BETWEEN OBSTRUCTIVE & RESTRICTIVE LUNG PATHOLOGIES

	Obstructive lung disease	Restrictive lung disease
Residual volume	• INCREASE	• DECREASE
Total lung capacity	• NORMAL/INCREASE	• DECREASE
Diffusion capacity	• NORMAL	• DECREASE
Vital capacity	• DECREASE	• DECREASE
Forced expiratory flow rate (FEF 25-75%)	• DECREASE	• NORMAL
FEV₁/FVC	• DECREASE	• NORMAL/INCREASE
DISEASES	- Asthma - Bronchiectasis - Bronchiolitis - Cystic fibrosis - COPD - Emphysema	- Parenchymal disorders like sarcoidosis, pneumoconiosis, idiopathic fibrosis, drug induced - Neuromuscular disorders like diaphragmatic palsy, GBS, muscular dystrophy - Chest wall disorders like Kyphoscoliosis, obesity, Ankylosing spondylitis

PATHOGNOMIC FOR:

- Restrictive disease-** decreased lung volumes like TLC & VC
- Obstructive disease-** decrease in Forced expiratory flow rate (FEF 25-75%) & FEV₁/FVC

COMPLIANCE:

- stretchability of the lungs, measured as change in lung volume per unit change in airway pressure (V/P). Normal value is **0.2L/cm H₂O**.
- Increased in: **Emphysema**
- Decreased in: **ILD, ARDS, Thorax deformities like kyphosis, scoliosis, pleural effusion, fibrosis etc...**

VENTILATION PERFUSION RATIO

- [V/Q= pulmonary ventilation/ pulmonary blood flow]

	Apex of the lung	Base
Ventilation	• Minimum	• Maximum
Perfusion	• Minimum	• Maximum
V/Q ratio	• Maximum (more prone for TB)	• Minimum

EFFECT OF GRAVITY ::

- In the upper portion of lungs, the blood flow is less, the alveoli are larger and ventilation is less than at base. The pulmonary arterial pressure is just sufficient to maintain.
- In the middle portions, the pulmonary arterial & capillary pressure exceeds alveolar pressure, but the pressure in the pulmonary venules may be lower than the alveolar pressure & may be collapsed during expiration. Beyond the constriction, blood falls into the pulmonary veins, which are compliant & take whatever amount of blood the constriction lets flow into them. This is called **WATER FALL EFFECT**.

RESPIRATORY REFLEXES

Head's paradoxical reflex	Hering-Breuer reflexes		J – receptor reflex (discovered by A.J.Paintal)
	Inflation reflex	Deflation reflex	
• -Vigorous inflation of	• - over stretching of the	• -over deflation of	• -receptors situated in alveolar

DMA'S CORNER OF WISDOM

the lung → reflex contraction of the diaphragm → further inflation • -mediated by Irritant receptors	lungs → stretch receptors send signals → respiratory neurons → switching off inspiratory centre → prolongs expiration	lungs → vagus stimulation → decrease in the duration of expiration	interstitium close to the capillaries. • - On stimulation leads to apnea, hyperventilation, bradycardia, hypotension etc...
---	---	--	--

Airways and lung receptors

Vagal innervation	Type	Location in interstitium	Stimulus	Response
Myelinated	• Slowly adapting	• Among airway smooth muscle cells	• Lung inflation	• *Inspiratory time shortening • *Hering-Breuer inflation and deflation reflexes • *bronchodilation • *tachycardia • *hyperpnea
	• Rapidly adapting	• Among airway epithelial cells	• Lung hyperinflation • Exogenous & endogenous substances like histamine, PGs	• *Cough • *Bronchoconstriction • *Mucus secretion
Unmyelinated C fibers	• Pulmonary C fibres • Bronchial C fibres	• Close to blood vessels	• Lung hyperinflation • Exogenous & endogenous substances like histamine, PGs	• *Apnea followed by rapid breathing • *Bronchoconstriction • *Bradycardia • *Hypotension • *Mucus secretion

CYANOSIS

- Due to increased quantity of reduced Hb (>5g/dl).

Central cyanosis	Peripheral cyanosis
• -both skin & mucus membranes are affected. • - due to ↓SaO₂ or presence of abnormal Hb	• -Mucus membranes are spared • - Due to slowing of blood flow & abnormally ↑ed O₂ extraction
• Methemoglobinemia • Sulphemoglobinemia • Carboxyhemoglobinemia • High altitude • Impaired pulmonary function • Anatomic shunts	• ↓ed cardiac output • Arterial/venous obstruction • Cold exposure • Redistribution of blood flow from extremities

CO POISONING

- CO has 200 times more affinity for Hb than oxygen
- Carboxy Hb cannot bind with Oxygen
- Leads to anemic hypoxia
- ODC is shifted to the left
- ABG: **normal PO₂, ↓SaO₂, variable PCO₂ & metabolic acidosis**
- Cherry red colour of skin & mucus membranes
- Treatment: Administration of oxygen at 10L/min

DMA'S CORNER OF WISDOM

HYPOXIA

- O₂ deficiency at the tissue level.

Type	Causes	Mechanism	P _A O ₂	P _a O ₂	O ₂ content	A-V difference
Hypoxic/ Anoxic/ Arterial (invariably involves the hippocampus)	• High altitude • Pneumonia	• Poor availability of O₂ for diffusion • Decreased Partial pressure of O₂ in arterial blood	↓	↓	↓	+
Anemic	• Anemia • CO Poisoning	• -Decreased O₂ carrying capacity of the blood due to quantitative or qualitative deficiency of Hb	+	+	↓	+
Stagnant/ Ischemic	• Cardiogenic shock	• O₂ content of the blood is exhausted due to reduction in blood velocity	+	+	+	↑
Histo Toxic	• Beriberi • HCN poisoning	• Tissue cannot make use of available O₂	+	+	+	↓

Best test for hypoxia:

- Hypoxic hypoxia- partial pressure of arterial O₂, treated by oxygen therapy.
- Anemic hypoxia- oxygen content (Hb %)
- Stagnant hypoxia- A-V difference [**increased**]
- Histotoxic hypoxia- A-V difference or PO₂ of venous blood [**decreased**]

Effects:

- Vasoconstriction of all blood vessels except that of pulmonary & cerebral circulation
- Hyperventilation due to decreased Partial pressure of O₂
- Increased sympathetic discharge
- Lactic acidosis
- Hypotension & tachycardia

NON-RESPIRATORY FUNCTIONS OF THE LUNGS

Synthesized & used in the lungs	Synthesized & released to blood	Partially removed from the blood	Activation in the lungs	Passes through the lungs without metabolism
○ Surfactant	○ Prostaglandin ○ Histamine ○ Kallikrein	○ Nor epinephrine ○ Bradykinin ○ Ach ○ Serotonin ○ Prostaglandin	○ Angiotensin-I → Angiotensin-II	○ Angiotensin -II ○ Adrenaline ○ Dopamine ○ Oxytocin ○ Vasopressin

REGULATION OF RESPIRATION

- Major stimulus for **spontaneous respiration & spontaneous breathing pattern** is CO₂.

NEURAL CONTROL		CHEMICAL CONTROL	
Medullary system	Pontine & vagal influences	Carotid & aortic bodies	Chemo receptors in brain stem
○ Pre-Botzinger complex: ○ -rhythm of respiration ○ (pace maker of respiration)	○ switching between inspiration & expiration ○ *Pneumotaxic centre: ○ -Nucleus Para Brachialis (NPB) ○ -switching between	○ Contain 2 types of cells. ○ Type-I (glomus) cells: are closely associated with cup like endings of the afferent nerves. ○ Type-II (glial) cells:	*Located in the ventral surface of the medulla *directly monitor the CSF [H⁺] and CO₂.

DMA: 291/139, 3rd floor, Thambu Chetty ST, Parrys, Chennai -01
Phone number: 044-42009468 **Mail us:** studyatdma@gmail.com
Web: www.dma-study.com & www.jzmustudy.com

DMA'S CORNER OF WISDOM

	inspiration & expiration. ○ *Apneustic centre: ○ -lower pons ○ -has an intrinsic rhythm, promotes prolonged inspirations when active.	supportive cells • Hypoxia is the potent stimulus. • Dopamine appears to be the predominant neurotransmitter via D2 receptors. • Carotid bodies more effective than aortic bodies	* CSF [H⁺] is the potent stimulus to central chemo receptor. *As the BBB is freely permeable to CO ₂ , these receptors respond slowly to changes in systemic arterial PCO ₂ .
○ Dorsal respiratory group (DRG): • -Nucleus Tractus solitarius(NTS) • -Site of origin of rhythmic inspiratory discharge.(Inspiratory ramp signals)	○ Vagus: Stretching of lungs during inspiration ↓ Stimulates afferent pulmonary vagal fibres ↓ Inhibit inspiratory discharge	○ Afferents from carotid body (most important peripheral chemo receptor) ascend to medulla via carotid sinus & glossopharyngeal nerves. ○ Afferents from aortic body ascend to medulla via vagus	
○ Ventral respiratory group(VRG): • -Nucleus Retro Ambiguus (NRA) • -Both inspiratory & expiratory control • -Inactive during normal quiet respiration		○ These receptors monitor PO ₂ & not O ₂ content. ○ Powerful stimulation is produced by cyanide & not by Anemia/CO poisoning	

- **There are no central PO₂ receptors**
- **Peripheral chemo receptors respond to ↓ PO₂ ↑ PCO₂ & H⁺ of arterial blood**

Applied physiology

HIGH ALTITUDE

- Sickness mainly due fall in total barometric pressure & PO₂.
- **Hypoxic hypoxia**
- Develops in 8-24 hours and lasts for 4-8 days.
- **Pathogenesis:** Low PO₂ → stimulates arterial chemo receptors → increase in pulmonary ventilation → blows off CO₂ → inhibits brain stem respiratory centre → respiratory distress.
- **Clinical features:** pulmonary edema & cerebral edema
- Life is **impossible without pressurization** at an altitude greater than **14000m**.
- Body **fluids boil** at an altitude of **19000m** at 37°C.

ACCLIMATIZATION:

- Development of compensatory mechanisms so that the effects of hypoxia are ameliorated.
- **Features:**
 - ✓ Hyper ventilation
 - ✓ Polycythemia
 - ✓ Increased oxygen diffusion
 - ✓ Increased cellular mitochondria
 - ✓ Increased 2,3 DPG

DMA: 291/139, 3rd floor, Thambu Chetty ST, Parrys, Chennai -01
Phone number: 044-42009468 **Mail us:** studyatdma@gmail.com
Web: www.dma-study.com & www.jzmustudy.com

DMA'S CORNER OF WISDOM

DECOMPRESSION SICKNESS

- Due to rapid return of a person to normal surrounding after exposure to high atmospheric pressures.
- Also called **caisson's disease/bend's or diver's palsy/ Dysbarism**
- Due to sudden return to atmospheric pressure, the N₂ is decompressed & escapes from the tissues, forming bubbles & causing air embolism.
- Prophylaxis: using SCUBA (Self Contained Underwater Breathing Apparatus).
- Treatment: slow decompression.

ABNORMAL RESPIRATORY PATTERNS:

Pattern	Cause	Mechanics
Cheyne – stokes respiration	• -Opium poisoning • -Uremia • -CCF • -Hypoxia	• Periodic breathing due to Rhythmic alteration of apnea & hyperpnea. • * waxing & waning tidal volume
Biot's breathing (Irregularly irregular breathing)	• Meningitis	• Periodic breathing with one or more large tidal volumes separated by apnea.
Kussmaul's respiration (Air hunger)	• -DKA • -Uremia	• Rapid & deep breathing
Ondine's curse	•	• Loss of spontaneous breathing with only voluntary control.

CYSTIC FIBROSIS (Chr.7)

- AR disorder, defect in a transport protein causing an abnormality in Cl transport in the apical membrane of airway epithelial cells. Most common mutation leading to CF is loss of Phenyl Alanine residue at position 508 of the protein $\Delta F508$.
- The gene product is called Cystic Fibrosis Transmembrane Conductance Regulator (CFTR)

PULMONARY EDEMA: (fluid in the pulmonary interstitium)

○ Normal pulmonary artery pressure	○ 25/10 mm Hg
○ Mean pulmonary artery pressure	○ 15 mm Hg
○ Normal pulmonary capillary pressure	○ 10 mm Hg
○ Increased pulmonary wedge pressure if	○ >18 mm Hg

DMA'S CORNER OF WISDOM

GASTRO INTESTINAL PHYSIOLOGY

Historical back-up...

- The term 'hormone' was coined by E.H.Starling to describe the actions of secretin.

ENTERIC NERVOUS SYSTEM (brain of the gut)

- Myenteric/Auerbach's plexus: regulates gut motility
- Sub-mucosal/Meissner's plexus: regulates blood flow & secretion

REGULATION OF GI FUNCTIONS

Nervous control:

Sympathetic	Para- sympathetic
-Increase in sympathetic activity slows processes	- Increase in Para- sympathetic activity promotes digestive & absorptive processes.
-decreases the motility & secretions. -Increases sphincter constrictions	- Increases the motility & secretions. -Decreases sphincter constrictions

Endocrine control:

Hormone	Source	Stimulus	Stomach	Pancreas	Gall bladder	Special features
Secretin	S cells of duodenum	Acid in the duodenum. Products of protein digestion	Inhibits gastric motility & Secretion	Stimulates HCO ₃ secretion		
	- Augments the activity of CCK in production of alkaline rich secretion of the pancreas. - Causes pyloric sphincter contraction along with CCK.					
Chole cystokinin (CCK)	Cells lining the duodenum & jejunum (I cells)	Fats & amino acids in the duodenum	Inhibits gastric emptying	Stimulates enzyme secretion	GB contraction -Relaxation of Sph.of Oddi	-major humoral mediator of meal stimulated enzyme secretion
	- CCK enhances small intestinal & colonic motility. - Increases the secretion of insulin & glucagon.					
Gastrin	G cells of the stomach- Antrum & Duodenum	Distension of the stomach	Stimulates gastric motility & Secretion of acid & pepsin	Stimulates insulin & glucagon secretion		Acid in the stomach inhibits secretion
GIP	Duodenum	Fat, Carbohydrates, Amino acids	Inhibits gastric motility & Secretion			

Stimuli that increase acid & Gastrin secretion	Stimuli that decrease acid & Gastrin secretion
- Distension - peptides - Calcium - Adrenaline - increased vagal discharge	- Acid - Somatostatin - Secretin - glucagon - VIP - Calcitonin

DMA'S CORNER OF WISDOM

Others:

- **Peptide-YY**: released from jejunum, inhibits gastric secretion & motility.
- **Ghrelin**: secreted by stomach, central control of food intake.
- **Substance-P**: found in endocrine & nerve cells of GIT, increases small intestinal motility.
- **GRP (analogue of Bombesin)**: present in vagal endings that terminate on G cells, increases gastrin secretion.
- **Guanylin**: acts in a paracrine fashion, produced by cells from pylorus to rectum, has molecular mimicry with enterotoxin of certain diarrhea producing strains of E.Coli.

MOTILITY

- Pace maker activity (**Basal Electrical Rhythm**) is responsible for intrinsic motor activity. Pace maker cells are the interstitial cells of Cajal, present in the circular muscle layer.

Region	BER
Stomach	3-4/min
Duodenum	12/min
Ileum	8/min
Caecum	6/min
Proximal colon	2/min
Sigmoid colon	6/min

	In intestinal cells	In other cells
Depolarization	• Ca^{2+} influx	• Na^{+} influx
Repolarisation	• K^{+} efflux	• K^{+} efflux

Swallowing:

- Reflex controlled by the brain stem via vagus.
- The events are: Relaxation of upper esophageal skeletal muscle sphincter → primary peristaltic wave → Relaxation of LES → relaxation of proximal stomach (**receptive relaxation**).

Mechanisms that prevent GE Reflux:

- Tonic activity of LES
- Valve mechanism of short portion of diaphragm that extend into the diaphragm.
- Pinch cock like action of rural fibres of the diaphragm.

ENTERIC REFLEX

- Forms the **basis** of peristaltic movement.
 - Most important feature is that the **sensory neurons feed information** into chains of **excitatory interneurons** that are linked in an aborally direction and also into **inhibitory interneurons**, that are linked ab-annaly
 - **As a result, activation of sensory fibers initiate a contraction 'behind' the site of stimulation relaxation 'in front' of the site of stimulation.**
- **SECRETORY REFLEX** the same principle, with the main difference that output (motor) pathways target the **secretory cells** of the gut, or the **blood vessels**.

LONG-RANGE REFLEXES

- Altogether different types of reflexes
- Involve **co-ordinated response of one region of the gut wall** following **activation in other parts** of the GIT.
 1. **Gastro-enteric reflex** – Distension of stomach = Increase the excitability (motor and secretory) of the small intestine.
 2. **Gastro-ileal reflex** - Distension of stomach = Intensifies the activity of the terminal ileum Opens the ileo-cecal sphincter

DMA'S CORNER OF WISDOM

- 3. Gastro- and duodeno-colic reflexes-** With participation of Extrinsic innervation And also hormonal (gastrin') Distension of stomach or duodenum=Initiate 'mass movements' of the colon.
- 4. Ileo-gastric reflex** –Distension of an ileal segment=Inhibits gastric motility.
- 5. Intestino-intestinal reflex** – Upon excessive distention (adynamic ileus), Rough handling (surgery) & Peritonitis (severe irritation) =Cessation of intestinal motility

Gastric motility:

- Contraction of the distal stomach by the BER wave is called Antral systole (4/min).
- **Stimulation:** Local Distension, Increased Para sympathetic activity via Ach & **Gastrin** release, Nicotine, histamine
- **Inhibition:** Acidity (by inhibiting Gastrin), duodenal overload, **CCK, Secretin, GIP, Somatostatin, Adr, NA, Atropine**
- Stomach Emptying: Liquids> Carbohydrates> Protein> fat. (Very slow for fatty foods)

Migrating motor complex: (House-keeper of the small intestine)

- Propulsive movements initiated during fasting & inter digestive periods,
- Begins in the stomach
- Moves undigested material in aboral direction at a rate of 5cm/min
- Repeats every 90-120 minutes in fasting.
- Facilitated by Motilin (**Secreted by entero chromaffin cells & Mo cells** in the stomach, small int & colon).

Small intestinal motility:

- Mixing – **Segmentation** (most frequent movement in the digestive state in small intestine)
- **Tonic contractions-** prolonged contractions that isolate one segment of the intestine from the other.
- **Propulsive-Peristalsis** (hastens transit in the GIT in the digestive state)
 - **Stimulus for peristalsis: distension of the gut**
 - **Rate of peristalsis: 2-25cm/min.**

Ileo caecal sphincter:

- Distension of ileum- Relaxation of sphincter.
- Distension of Colon- Contraction of sphincter.

Colon motility:

- Segmental contractions (haustrations), peristalsis & mass movements.
- Simultaneous contraction of the smooth muscles over large confluent areas- Mass action contractions occur only in the colon.

Digestive motility	Interdigestive motility	Propulsive movement	Mixing movement
○ Peristalsis	○ MMC	○ Peristalsis	○ Segmentation
○ Segmentation		○ MMC	○ Haustral shuttling
○ Haustration			

Defecation reflex:

- Integrated at **spinal cord**.
- First urge to defecate occurs when the rectal pressure exceeds 18mmHg
- At 55mmHg both the internal & external sphincters relax & expulsion occurs.

Gastro colic reflex:

- Distension of the stomach → contractions of the rectum → desire to defecate
- Mediated by gastrin

Transit time: (time taken for the test meal to reach a particular site)

DMA: 291/139, 3rd floor, Thambu Chetty ST, Parrys, Chennai -01
Phone number: 044-42009468 **Mail us:** studyatdma@gmail.com
Web: www.dma-study.com & www.jzmustudy.com

DMA'S CORNER OF WISDOM

- Caecum-4 hours; Hepatic flexure- 6 hours
- Splenic flexure- 9 hours; Pelvic Colon-12 hours

SECRETIONS:

SALIVARY

- Mediated by Para sympathetic stimulation. **Low in Na & Cl** with high K & HCO₃. Hypotonic due to re-absorption of NaCl.
- α – Amylase (ptyalin): **begins carbohydrate digestion.**

Composition of saliva

- Saliva is characterized by:
 - **High volume (relative to the small of the salivary glands)**
 - **High K⁺ and HCO₃⁻ concentrations**
 - Low Na⁺ and Cl⁻ concentrations
 - Hypotonicity
 - Presence of amylase, lingual lipase, and kallikrein

The composition of saliva varies with the salivary flow rate

- **At the lowest flow rates**-- saliva has
 - Lowest osmolarity Lowest Na⁺, Cl⁻, and HCO₃⁻ concentrations
 - Has the **highest K⁺ concentration.**
- At the highest flow rates= up to 4 ml/min composition of saliva is closet to that of plasma
- Salivary gland formed by three major glands
 - Parotid
 - Submaxillary
 - Sublingual glands.

GASTRIC

- **Parietal (Oxyntic) cells:** present in the body of stomach. Secrete HCl & Intrinsic factor [combines With Vit-B₁₂ & reabsorbed in distal ileum]
- **Chief (Zymogen/peptic) cells:** present in the body & fundus of stomach. Secrete Pepsinogen, converted to pepsin by acid. Pepsin **begins the digestion of protein.**
- **Mucus cells:** secrete mucus, HCO₃. Stimulated by prostaglandins. Protects the stomach.
- **Gastric secretions are the most acidic of entire GIT.**
- **Phases of gastric secretion:**
 - **Cephalic phase-** mediated by vagus. Abolished by vagotomy & atropine
 - **Gastric phase-** induced by food in the stomach
 - **Intestinal phase-** feedback inhibition on gastric secretion initiated from intestinal mucosa.

Contents of gastric juice:

- Pepsin
 - Lipase
 - Mucus
 - Intrinsic factor
 - Acid
 - Ions like Mg²⁺, Na²⁺, K⁺, H⁺ & Cl⁻, HPO₄²⁻, SO₄²⁻
- **VOMITING→ Hypokalemia & metabolic alkalosis**

PANCREATIC:

- Amylases: hydrolyses carbohydrates

DMA: 291/139, 3rd floor, Thambu Chetty ST, Parrys, Chennai -01
Phone number: 044-42009468 **Mail us:** studyatdma@gmail.com
Web: www.dma-study.com & www.jzmustudy.com

DMA'S CORNER OF WISDOM

- Lipases: **begins fat digestion**. Digests fat to 2 FFAs & 1 monoglyceride.
- Esterases: hydrolyses cholesterol esters into cholesterol & FFAs.
- Enterokinase, an enzyme secreted by the lining cells of small Intestine activates pancreatic enzymes like trypsinogen, chymo trypsinogen & Carboxy peptidase.

- **Pancreatic secretions are the most alkaline** as it secretes high amounts of HCO_3^- .
- **COLON:** Secretion of HCO_3^- & K^+

BILE METABOLISM

- Primary bile acids- Cholic & Cheno deoxy cholic acid.
- Secondary bile acids- deoxycholic & lithocholic acids.
- Cholic acid is abundant.
- **Cholerectics**- stimulate bile secretion. Bile salts are most potent. Others are secretin & vagal stimulation
- **Cholagogues**- increases bile flow by GB contraction.
- **Mainly CCK**. Others are fatty acids & amino acids
- Daily bilirubin formation- 250-350mg
- 1 gram of Hb yields 35mg of bilirubin.
- Total circulating bile salt pool is approximately-3.5g.
- Entero-hepatic circulation occurs 6-8 times/day.
- Normal rate of bile salt synthesis -0.2-0.4g/day

ABSORPTION

Carbohydrate:

- Luminal Side- glucose & galactose absorbed by secondary active transport.
- Basal side- Absorbed passively by facilitated diffusion
- Fructose is absorbed independently.
- The maximal rate of glucose absorption from the intestine is: 120g/hour

Protein:

- Luminal Side- absorbed by secondary active transport linked to Na^+ & receptor mediated endocytosis.
- Basal side- simple diffusion of amino acids

Lipids: short chain fatty acids- simple diffusion directly into blood stream, others via thoracic duct.

- Glucose- middle small intestine
- Amino acids-- small intestine
- Fat- small intestine except small chain fatty acids.
- Small chain fatty acids- Colon
- Ions- upper small intestine
- Fat soluble vitamins - upper small intestine
- Water soluble vitamins except B-12- upper small intestine
- Iron-duodenum
- Water-jejunum
- B_{12} & IF- distal ileum
- Bile acids- distal ileum

ENERGY KINETICS:

- Energy released by combustion of food stuffs is measured by a **bomb calorimeter**.
 - **Carbohydrate**-4.1kcal/kg
 - **Fat**-9.3kcal/kg
 - **Protein**- 5.3kcal/kg.
- **But the oxidation of protein is incomplete in our body. Hence its calorific value in the body is only 4.1kcal/kg**

DIETARY FIBRE

- All ingested food that reaches the large intestine in unchanged form.
- **Components:** Cellulose, hemi-cellulose, Pectin, lignin & gums.
- **Advantage:**
 - reduces the stool transit time
 - Reduces the incidence of Ca.Colon, DM, CAD, and Diverticulitis.

DMA: 291/139, 3rd floor, Thambu Chetty ST, Parrys, Chennai -01
Phone number: 044-42009468 **Mail us:** studyatdma@gmail.com
Web: www.dma-study.com & www.jzmustudy.com

DMA'S CORNER OF WISDOM

ENDOCRINOLOGY AND REPRODUCTION

Historical back up:

- (Bayliss & Starling-1902) identified the first hormone **Secretin**
- Coined the term hormone (to excite)
- Sandstrom -1877- Discovered the parathyroid gland.
- Paul Langerhans 1868- discovered the pancreatic islets.
- Best & Banting -1921- Discovered insulin.
- Steptoe & Edwards-1978- In Vitro Fertilization. (IVF)

Cellular links

Types	Mediated by
○ Autocrine	○ Hormones acting on the same cells that release them
○ Paracrine	○ Hormones acting locally without entering circulation
○ Neurocrine	○ NT's acting in the synaptic junctions
○ Endocrine	○ Hormones acting on target cells at distant sites
○ Local hormones	○ Acts at the site of release. eg: Ach, also called as autacoids
○ Pheromones	○ Released into the environment (animals)

Types of hormones and their mechanism of action:

Hormones	Mechanism of action	Examples
Protein hormones & catecholamines	• Combines with cell surface receptors and may • Increase adenylyl cyclase activity via G proteins & increases intracellular cAMP. • Modify guanylate cyclase activity via G proteins & alters intracellular cGMP • ↑ intracellular Ca^{2+} / IP_3 / DAG • ↑ kinase/ Phosphatase activity	• Calcitonin, ACTH, PTH, Glucagon, LH, FSH, ADH, TSH, Somatostatin • NO, ANP • Oxytocin, Ach, GnRH • Insulin, Prolactin, GH, IGF-I & II
Steroid hormones	• Binds & forms a complex with cytoplasmic receptor. Complex enters the nucleus & regulates protein synthesis.	• Androgen, Estrogen, Progesterone, Cortisol • Aldosterone, Vit-A & D
Thyroid hormones	• Binds & forms a complex with nuclear receptor & regulates protein synthesis	• Thyroxine

G-Proteins:

- They have 3 sub units (α , β , γ)
- Each sub unit is distinct.
- They are guanylyl nucleotide (GTP/GDP) binding proteins
- The α sub unit has inherent GTPase activity
- The β and γ subunits are coupled to effectors molecules like adenylyl cyclase, ion channels.
- GPCR have seven transmembrane domains and span the membrane seven times. thus they are often called **seven-helix receptors or serpentine receptors**
- There are several types of G proteins; **G_s** is stimulatory G protein and it activates adenylyl cyclase. **G_i** is inhibitory protein and it inhibits adenylyl cyclase; Activation of **G_q** leads to activation of the membrane bound enzyme phospholipase C.
- Other families of proteins such as **ras** resemble G-proteins in structure and function.
- Nephrogenic DI, Familial hypercalciuric hypercalcemia, Testotoxicosis, some malignancies are G protein related disorders.

DMA'S CORNER OF WISDOM

Drugs/toxin used in G-protein research:

Drug/toxin	Mechanism of action
○ Cholera toxin	○ ADP-ribosylation of α subunit of G_s , activation of adenylate cyclase
○ Pertussis toxin	○ Inhibition of α subunit of G_i
○ Forskolin	○ Directly activates adenylate cyclase

THYROID HORMONES (Calorigenesis)

- **Synthesis:** in follicular cells of thyroid gland by iodination of tyrosine.
- **Steps:** Iodide trapping (by Na-I pump) → Oxidation of iodide to iodine (by peroxidase) → Iodination of tyrosine (by peroxidase) to form MIT, DIT → coupling of iodinated tyrosine to form thyronine (T_3 & T_4) → **storage** → release.
- **Transport:** by binding to plasma proteins:
 1. Thyroid binding globulin (TBG)(90%)
 2. Thyroid binding pre-albumin(TBPA)/Transthyretin
 3. Albumin

T_4 (transport form)	T_3 (active form)
• Secretion by the gland is more.	• More potent.
• Major circulating hormone.	• Acts faster than T_4
• More tightly bound to plasma proteins	• More tightly bound to nuclear receptors
• Half life is more(6-7 days) than T_3 (1-2 days)	• About 1/3 of T_4 is converted to T_3 in peripheral tissues.

- **NOTE:**
 1. Iodine uptake is also seen in salivary gland, mammary gland, placenta, gastric mucosa, ciliary body of the eye. Their uptake is not influenced by TSH & they won't produce thyroxine.
 2. Thyroid is the only endocrine gland that can store a large amount of hormone for future release.
- **Mechanism of action:** by binding to nuclear receptors. (Increases the activity of Na^+K^+ pump & uncoupling of oxidative phosphorylation).
- **Normal values:**
 - **Total body iodine**-50mg, 10-15 mg in thyroid gland
 - T_4 -4 to 11 $\mu g/dl$;
 - T_3 - 0.07 to 0.2 $\mu g/dl$;

Physiological effects of thyroxine (mostly mediated by T_3)

Oxidative metabolism	○ *T_3 stimulates O_2 uptake in all tissues except brain, uterus, lymph nodes, spleen, ant. pituitary & testes. ○ * Increased BMR & Calorigenesis
Carbohydrate metabolism	○ * Increases blood sugar by $\uparrow$ ing gut absorption, glycogenolysis & neoglucogenesis, producing a diabetic state called metathyroid diabetes.
Lipid metabolism	○ *Reduces serum cholesterol by $\uparrow$ing its biliary excretion ○ *$\uparrow$es lipolysis & FFA in blood
Protein metabolism	○ * Both anabolism & catabolism. Under physiological conditions, anabolism predominates.
Skeletal system	○ * Helps in bone growth & maturation
CNS	○ *Enhances brain development in fetal & Postnatal period. ○ *α wave frequency in EEG increased in hyperthyroidism ○ *favors myelination.
CVS	○ * $\uparrow$ es myocardial contractility, HR, CO, Sys B.P, Pulse pressure.
Temperature	○ *$\uparrow$es calorigenesis & heat production. ○ *mediates calorigenic activity of adrenaline.
Other effects	○ *Essential for normal gonadal functions. * $\uparrow$ es lactation

DMA'S CORNER OF WISDOM

Thyroid disorders:

- **Hypo secretion:**
 - **Cretinism**- in children (retardation of physical growth & mental development- hallmark of congenital hypothyroidism)
 - **Myxedema**- in adults (accumulation of mucoproteins in subcutaneous tissues).
- **Hyper secretion:**
 - **Goiter**
 - **Thyrotoxicosis**
 - **Thyrotoxic crisis/ Thyroid storm:** fever, tachycardia, hypotension, vomiting & diarrhea. Produced by stress, infection, surgery etc...
- **Causes of congenital hypothyroidism:**
 - a. Maternal iodine deficiency
 - b. Fetal thyroid dysgenesis
 - c. Fetal hypopituitary hypothyroidism
 - d. Maternal thyroid antibodies that crosses the placenta
 - e. Inborn errors of thyroid hormone synthesis.
- **CALCITONIN:** The Para follicular cells of the thyroid gland secrete Calcitonin which plays a role in regulating calcium metabolism. Its secretion is increased by hypercalcemia, hyper gastrinemia, and β adrenergic agonists
- **Salmon Calcitonin:** produced by ultimobronchial bodies, is more effective than Calcitonin.

PARATHYROID HORMONE (calcium metabolism)

- **Synthesis:** by principal/ chief cells of parathyroid gland. Mainly regulated by serum Ca^{2+} levels. No influence from the pituitary.
- **Calcium Metabolism:**
 - ✓ Total body calcium-1gram of which 99% is in bones.
 - ✓ Normal serum calcium: 5mEq/L or 2.5mmol/L or simply 9-10.5 mg/dl.
 - ✓ Normal dietary requirement: 0.5 to 1g.

Types of calcium:

Diffusible/ultra filterable (5.5mg/dl)	Non-diffusible/protein bound (4.5mg/dl)
● Ionized calcium (4.5mg/dl)	● Albumin bound(4mg/dl)
● Complexed with other minerals (0.5mg/dl)	● Globulin bound(0.5mg/dl)

- Ionized calcium (4.5mg/dl) is responsible for many functions such as muscular contraction, NT release, coagulation etc...
- Maximum calcium absorption occurs in **duodenum & proximal jejunum**, facilitated by gastric acid.
 - **Absorption ↑ed by** –Acidic pH, hypocalcaemia, proteins
 - **Absorption ↓ed by** Achlorhydria, phosphates, oxalates, alkalis, hypercalcemia.

Hormones involved in calcium metabolism:

FEATURES	PTH	VITAMIN-D	CALCITONIN
Stimulus for release	↓ serum Ca^{2+}	↓ serum Ca^{2+} ↓ serum P ↑PTH	↑ serum Ca^{2+}
Receptor location	Osteoblast	Osteoblast	Osteoclast
Action on:			
Bone	↑ resorption	↑ resorption	↓resorption
Kidney	↓ P reabsorption ↑ Ca^{2+} reabsorption (in distal tubule)	↑ P reabsorption ↑ Ca^{2+} reabsorption	
Intestine	↑ Ca^{2+} absorption (by activation of vit-D)	↑ P absorption ↑ Ca^{2+} absorption	
Over all effect on:			
Serum calcium	↑	↑	↓
Serum phosphorus	↓	↑	↓

DMA'S CORNER OF WISDOM

Other Hormones involved in calcium metabolism:

- **Thyroid hormone & Glucocorticoid excess:** ↓ serum Ca^{2+} and leads to osteoporosis.
- **Growth hormone:** ↑ urinary Ca^{2+} excretion
- **Oestrogens & testosterone** - Prevent osteoporosis.

Disorders of calcium metabolism:

- **Hypoparathyroidism:** Tetany- due to reduced serum ionic calcium & not total Calcium.
- Symptoms: carpopedal spasm, neuromuscular hyper excitability, laryngismus stridulus,
- Tetany may also be due to alkalosis, Vit-D & Mg^{2+} deficiency, citrate and HCO_3^- therapy.
- **Latent Tetany**- elicited by Trousseau's sign, Chvostek's sign.
- **Pseudo Hypoparathyroidism:** Target tissues are resistant to PTH.
- **Hyperparathyroidism:** Hyper calcemia, hypo phosphatemia, formation of bone cysts (Osteitis fibrosa cystica), renal stones etc.

ADRENAL MEDULLA (not essential)

- Made of chromaffin cells
- **Two types of cells**
 - 90%- large cells- less dense granules, secrete adrenaline.
 - 10%-Small cells- more dense granules, secrete non adrenaline

Adrenaline(80% of adrenal output)	Nor adrenaline(20% of adrenal output)
○ Pre dominant in: dog, tense & anxious situations, unexpected emergencies, metabolic stress like hypoglycemia, pain & trauma	○ Pre dominant in: fetal life, cat, medullary tumors, active aggressive emotions, more familiar stress, asphyxia, hypoxia, circulatory stress except hemorrhage,
○ Acts on both α and β receptors	○ Predominant α action
○ *Heart: ↑ HR, CO, SBP, ↓TPR, ↓ DBP	○ Vasoconstriction except coronary vessels, ↑ TPR, SBP & DBP → ↑ MAP
○ Biphasic action on BP.	
○ *BV: Vasoconstriction except coronary vessels.	
○ *Smooth muscle relaxation & sphincter contraction.	
○ *Calorigenesis: only if thyroxine is +	
○ Orbeli phenomenon: Simultaneous stimulation of a somatic nerve during excitation of the motor nerve of a muscle increases the contraction.	

Mechanism of action:

- α_1 : increasing intra cellular Ca^{2+}
- α_2 : decreasing adenylate cyclase & intra cellular cAMP.
- $\beta_{(1+2)}$: increasing adenylate cyclase & intra cellular cAMP

ADRENAL CORTEX (essential for life)

Layer	Secretes	Hormones	Kinetics
Zona glomerulosa	• Mineralocorticoids	• Aldosterone (most potent) • Deoxy corticosterone	• 60% bound to albumin, • $T_{1/2}$ -20 mins
Zona fasciculata(widest)	• Glucocorticoids	• Cortisol (large amounts) • corticosterone	• 90% bound to α globulin called Transcortin, • $T_{1/2}$ -60 mins
Zona reticularis	• Androgens	• Dehydroepiandrosterone • Androstenedione	

DMA: 291/139, 3rd floor, Thambu Chetty ST, Parrys, Chennai -01
Phone number: 044-42009468 **Mail us:** studyatdma@gmail.com
Web: www.dma-study.com & www.jzmustudy.com

DMA'S CORNER OF WISDOM

Eosinophils, Lymphocytes(BEL), -Decrease the size of lymph nodes, -thymic atrophy. 8. Immuno suppression 9. Anti-inflammatory: 10. Connective tissue: -reduces fibroblastic activity. 11. Anti-allergic action: 12. Inhibits the secretion of ACTH,MSH,TSH,GH	neuro secretory cells of hypothalamus increases ACTH secretion. Stress, emotions, trauma & circadian rhythm leads to increased CRH release.	○ -Hypertension Nelson's syndrome: ○ Development of ACTH secreting pituitary tumor following adrenalectomy for Cushing's disease.
--	---	---

Changes following steroid therapy

CELLS	NORMAL	AFTER TREATMENT
Total WBC count	• 9000	• 10000
PMNs	• 5760	• 8330
Lymphocytes	• 2370	• 1080
Eosinophils	• 270	• 20
Basophils	• 60	• 30
Monocytes	• 450	• 540
RBCs	• 5 million	• 5.2 million

- **Note:** following steroid therapy, all the cell types' increase except BEL- Basophils, eosinophils, lymphocytes.

Congenital adrenal hyperplasia:

Types	Enzyme function	Mineralo corticoid activity	Glucocorticoid activity	Androgen activity	Features
3 β -hydroxylase deficiency	Aldosterone & Cortisol synthesis	↓	↓	↑	-Male hermaphrodite
11- β hydroxylase deficiency	Cortisol synthesis	↑	↓↓	↑	-Hypertension -Virilisation & precocious puberty in Females
17- α hydroxylase deficiency	Cortisol & androgen synthesis	↑	↓	↓↓	-Male hermaphrodite -Hypertension
21- β hydroxylase deficiency	Aldosterone & Cortisol synthesis	↓	↓↓	↑	-Hypotension - Virilisation in Females & precocious puberty in males

- **Hypertension:** 11-hydroxylase deficiency & 17-hydroxylase deficiency.
- **Male hermaphroditism:** 3 β -hydroxylase deficiency & 17-hydroxylase deficiency
- **Female hermaphroditism:** 11-hydroxylase deficiency & 21-hydroxylase deficiency
- **21-hydroxylase deficiency- m.c.cause for ambiguous genitalia of newborn (virilisation) & primary amenorrhea.**
- **Steroidogenic acute regulatory (StAR)** protein is essential for steroid synthesis in gonads & adrenals but not in the placenta. Mutation in the gene coding for this protein is a cause of severe congenital adrenal hyperplasia in newborns. In its absence only small amounts of steroids are formed.

PITUITARY HORMONES

Hormone secreting cells of anterior pituitary			
Acidophilic cells		Basophilic cells	
Cell type	Hormone	Cell type	Hormone
• Somatotrope	• Growth hormone	• Corticotrope	• ACTH

DMA: 291/139, 3rd floor, Thambu Chetty ST, Parrys, Chennai -01
Phone number: 044-42009468 **Mail us:** studyatdma@gmail.com
Web: www.dma-study.com & www.jzmustudy.com

DMA'S CORNER OF WISDOM

• Lactotrope	• Prolactin	• Thyrotrope • Gonadotrope	• TSH • FSH,LH
--------------	-------------	-------------------------------	-------------------

Pituitary regulation by the hypothalamus

Adenohypophysis (Ant.pituitary)	Neurohypophysis(Post.pituitary)
The hypothalamus releases tropic hormones into the hypophyseal portal circulation, as per negative feed back mechanism, which reaches the anterior pituitary & regulates its secretions	*Oxytocin & Vasopressin is synthesized in the supra optic & para ventricular nuclei of hypothalamus and released in the nerve endings(Herring bodies) of the hypothalamo-hypophyseal tract fibres in the post. Pituitary

Hormones of anterior pituitary and their actions:

Hormones	Features
GH (Somatotropin)	*actions mediated by somatomedins produced by liver, *growth of all tissues except fetal growth, sex organs, brain & hair. *protein anabolism & lipid catabolism, Hyperglycemia. 'Meta hypophyseal diabetes'. - promotes erythropoiesis & mineral retention. Secretion ↑by hypoglycemia, exercise, oestrogen, glucagon, vasopressin, thyroxine, Cortisol, aminoacidemia. Secretion ↓by hyperglycemia, FFA, somatostatin, cortisone, progesterone.
TSH	2 sub units α and β, α unit identical with FSH,LH,hCG Secretion ↑by TRH, oestrogen, decreased thyroid hormones Secretion ↓by Cortisol & Somatostatin
ACTH	* 39 AAs, Also increases MSH activity & lipolysis.
FSH	*females- Follicular development & oestrogen secretion * males- Spermatogenesis
LH	* Hormone of ovulation, secretion of progesterone & testosterone.
PROLACTIN	*Influenced by hypothalamus[PRH < PIH (dopamine).] - helps in breast development & lactation * Lactational amenorrhea

- NOTE:** In section of the pituitary stalk, the secretions of all the above hormones are decreased **except Prolactin.**

Hormones of posterior pituitary and their actions:

Hormones	Features
VASOPRESSIN	-synthesized in Supra-optic nuclei, bound to Neurophysin-II -↑es water reabsorption & retention. Mainly by V_2 receptors. & increasing cAMP - ↑es smooth muscle contraction by acting on V_1 receptors & increasing intracellular calcium.
OXYTOCIN	-synthesized in Para ventricular nuclei, bound to Neurophysin-I - Milk ejection, uterine muscular contraction during labor, sperm transport along genital tract.

APPLIED:

- Pituitary dwarfism:** Childhood GH deficiency. Stunted growth, delayed puberty.
- Laron dwarfism:** normal GH levels, un responsive target organs.
- Pan hypopituitarism- Sheehan's & Simmonds disease**(ant.pituitary degeneration).
- Gigantism-** hyper secretion in childhood, disproportionately long limbs, MR
- Acromegaly-** hyper secretion in adults, broadening & thickening of hands & feets, thickening of skin, hyperglycemia.
- Hyperprolactinemia:**
- Diabetes insipidus:** deficiency of vasopressin secretion.
- Nephrogenic DI**
- DIDMOAD/ wolfram syndrome**
- SIADH-** excess vasopressin secretion causes water retention & volume expansion but with hyponatremia & reduced plasma osmolality. Urine Osmolality is high. Also called **dilution syndrome.**

DMA'S CORNER OF WISDOM

PANCREATIC HORMONES

Pancreatic cell	Structure	Secretion
A (α) cells	20% of islets	Glucagon
B (β) cells	70% of islets	Insulin
D (δ) cells	5-8% of islets	Somatostatin (universal inhibitor)
F cells	Fewer in number	Pancreatic polypeptide
D – 1 cells		VIP

INSULIN (THE HORMONE OF FEAST)

Structure:

- Made of 51 amino acids (**A chain**-21 AA's & **B chain**-30 AA's)
 - Synthesized in ribosomes of rough ER of β cells.
 - Pre-pro insulin (107AA) $\rightarrow$ 23 AA's removed $\rightarrow$ folded & linked by disulfide $\rightarrow$ Proinsulin (84AA) $\rightarrow$ Insulin (51AA) + C-peptide (33AA).
 - Transported as free form, not bound to plasma proteins
- Measurement of C-peptide: indicator of the rate of insulin secretion.**
 - Average daily secretion 2mg (50 units), $T_{1/2}$ - 5 mins.**
 - Only hormone with hypoglycemic effect.**

INSULIN RECEPTOR:

- glycoprotein made up of 2 large α subunits & 2 smaller β subunits.
- α subunit**- located outside the CM & **β subunit**- traverses the CM & has tyrosine kinase activity.
- Present in all CM including those which do not need insulin for glucose entry.
- Excess insulin decreases & low insulin increases the number of receptors.

MECHANISM OF ACTION:

- Binding of insulin to the receptor $\rightarrow$ triggers tyrosine kinase activity $\rightarrow$ auto phosphorylation of β subunits $\rightarrow$ phosphorylation & dephosphorylation of cytoplasmic proteins.
- Growth promoting effects are mediated by phospho inositol -3 kinase.**

Glucose transporters in mammals:

Transporter	Function	Sites of expression
Secondary active transport		
SGLT-1	● Glucose Absorption	● Small intestines, renal tubules
SGLT-2		● renal tubules
Facilitated diffusion		
GLUT-1	● Basal glucose uptake	● Brain,RBC,Kidney, Colon, Placenta, BBB
GLUT-2	● β-cell glucose sensor, glucose transport in intestinal & renal epithelium	● β-cells of islets, liver, intestinal & renal epithelium
GLUT-3	● Basal glucose uptake	● Brain, Kidney, , Placenta
GLUT-4	● Insulin mediated glucose uptake	● Skeletal & Cardiac muscle, adipose tissues
GLUT-5	● Fructose transport	● Jejunum, Sperm
GLUT-7	● Glucose-6 Phosphate transporter in ER.	● Liver

Note:

- SGLT-2 specifically binds with d- glucose & the rate of transport of d-glucose is greater than l-glucose.
- Phlorizin**, a plant glycoside, competes with d-glucose to bind with SGLT-2

DMA'S CORNER OF WISDOM

ACTIONS OF INSULIN:

Adipose tissue	Muscle	Liver
-↑ glucose entry & Fatty acid synthesis. ↑ TGL deposition - Activates Lipoprotein lipase & ↑ clearance of VLDL & Chylomicrons. - Inhibits hormone sensitive lipase & inhibits lipolysis.	-↑ glucose entry & glycogen synthesis. -↑ amino acid uptake & protein synthesis -↑ ketone uptake & ↑ K^+ uptake	-↑ protein synthesis & fat synthesis - Inhibits gluconeogenesis & glycogenolysis
Other effects		
-↑ activity of Na K pump. -↑ K^+ entry into cell, - decreases Na uptake -Acceleration of growth		

RAPID(seconds)
Increased transport of glucose, amino acids & K^+ into cells
INTERMEDIATE (minutes)
- Stimulation of protein synthesis - Inhibition of protein degradation - Activation of glycolytic enzymes & glycogen synthase - Inhibition of phosphorylase & Gluco neogenic enzymes
DELAYED (hours)
Increase in mRNAs for lipogenic & other enzymes

○ **Substances with insulin like activity:**

- Insulin
 - Proinsulin
 - IGF-I & IGF-II (Low molecular weight fractions)
 - High molecular weight fractions (IGF bounded to plasma proteins).
- c & d are collectively said to have **Non Suppressible Insulin Like Activity.(NSILA)**

COMPARISON OF INSULIN AND INSULIN LIKE GROWTH FACTORS

	Insulin	IGF-I	IGF-II
Other names	...	Somatomedin C	Multiplication stimulating activity (MSA)
Number of amino acids	51	70	67
Source	Pancreatic B cells	Liver & other tissues	Diverse tissue
Levels regulated by	Glucose	GH after birth, nutritional status	Unknown
Plasma levels	0.3-2ng/ml	10-700ng/ml; peaks at puberty	300-800ng/ml
Plasma binding proteins	No	Yes	Yes
Major physiological role	Control of metabolism	Skeletal & cartilage growth	Fetal growth

Factors affecting insulin secretion:

Stimulated by	Inhibited by
-Glucose, Mannose -β keto acids -Amino acids like leucine, arginine	-α adrenergic stimulants -2 de oxy glucose & Mannoheptulose -β blockers

DMA: 291/139, 3rd floor, Thambu Chetty ST, Parrys, Chennai -01
Phone number: 044-42009468 **Mail us:** studyatdma@gmail.com
Web: www.dma-study.com & www.jzmustudy.com

DMA'S CORNER OF WISDOM

- β agonists
 - glucagon, GH, Glucocorticoids, prostaglandins
 - hyponatremia
 - secretin, gastrin, CCK
 - Theophylline
 - cAMP
 - Sulfonyl ureas
 - Vagal stimulation during hyperglycemia

- somatostatin, **insulin**
 - Diazoxide, Thiazides
 - Phenytoin
 - **hypo kalemia**
 - Alloxan
 - Vagotomy

EFFECTS OF HYPOGLYCEMIA:

- Complete inhibition of insulin secretion occurs below the blood sugar levels of **80mg/dl**.
- Glucagon, GH, Epinephrine secretion occurs below the blood sugar levels of **70mg/dl**.
- COMA- levels less than **30mg/dl**.
- CONVULSIONS- levels less than **20mg/dl**
- PERMANENT BRAIN DAMAGE & DEATH - levels less than **10mg/dl**

GLUCAGON (THE HORMONE OF FASTING)

Structure:

- Made of 29 amino acids, $t_{1/2}$ -5 to 10 mins.

Mechanism of action:

- Increasing adenylate cyclase & intra cellular cAMP

Actions:

- $\uparrow$ blood glucose level by $\uparrow$ glycogenolysis, gluconeogenesis, lipolysis.
- $\uparrow$ lipolysis & calorogenesis.
- **Glucagon is the most potent hepatic glycogenolytic substance & more active than Adr. Does not stimulate muscle glycogenolysis.**

TISSUE UTILISATION OF GLUCOSE:

- Metabolism of brain, RBC, fat, muscle-50%
- Storage as fat & protein-30-40%
- Storage as glycogen- 5%

APPLIED:

- DM:
 - $\uparrow$ ECF glucose & $\downarrow$ in intracellular glucose. (Cell Dry)
 - Excess H^+ ions and ketosis leads to DKA.
 - Acidosis stimulates respiratory centers & leads to Kussmaul breathing..
 - Acidosis & dehydration leads to coma.
- **HbA_{1c}**- for assessment of blood sugar levels of the previous 4-6 weeks. (Normal: 4-8%)
- **Fructosamine**: Glycosylated albumin, reflects sugar levels of preceding 1-3 weeks.
- INSULIN EXCESS: (insulin overdose/insulinoma)
 - Hypoglycemia (< **40 mg/dL**) affects cortical functions

Serum blood sugar levels & effects:

< 40 mg/dL	30 mg/dL	<30 mg/dL	<10 mg/dL
• Mild symptoms	• Coma & convulsions	• Irreversible brain damage	• Death

GROWTH

Cell types:

- **Labile cells**→ continuous cell replication throughout the life, eg. Skin epithelium, endometrium

DMA: 291/139, 3rd floor, Thambu Chetty ST, Parrys, Chennai -01
 Phone number: 044-42009468 Mail us: studyatdma@gmail.com
 Web: www.dma-study.com & www.jzmustudy.com

DMA'S CORNER OF WISDOM

- **Stable cells**→ discontinuous cell replication. Long life span, but divide only when suitably stimulated, Eg. Hepatocytes, epithelial cells of kidney, pancreas & endocrine glands.
- **Permanent cells**→ non replicators lost the ability to divide Eg: Cardiac cells, neurons.

○ Growth stimulators	• GH(Somatotropin), Thyroxine, Insulin, Androgens, • IGF-I (Somatomedin-C), EGF, PDGF, FGF, NGF.
○ Growth inhibitors(Chalones)	• Corticosteroids, TNF, TGF-β

○ **Pigment abnormalities in humans:**

- Albinism**- genetic defects in the pathways for melanin synthesis.
- Piebaldism**- occurs in patches, congenital defect in the migration of pigment cell precursors from the neural crest.
- Vitiligo**- occurs in patches, develops after birth, progressive.

GONADOGENESIS

Spermatogenesis	Oogenesis
Spermatogonium(2n) ↓ Mitosis Primary spermatocyte(2n) ↓ Meiosis Two Secondary spermatocytes(n) ↓ Two Spermatids(n) from each ↓ Spermatozoa(n) ○ *1 primary spermatocyte gives rise to 4 spermatids. ○ 1 Spermatogonium gives rise to 512 spermatids. ○ * It takes 74 days for the spermatogonium to become spermatozoa.	Oogonia(2n), ↓ Ist meiotic division in embryonic ovary, arrested in the stage of late prophase Primary Oocyte(2n) ↓ completion of Ist meiotic division, Just before ovulation Secondary Oocyte (n)+ Ist polar body ↓ IInd meiotic division, arrested At Metaphase. Oozoa (n)+ IInd polar body ○ The second meiotic division is completed only after the entry of sperm in to ovum ○ 1 primary Oocyte gives rise to one ovum

MALE REPRODUCTIVE SYSTEM:

- Spermatogenesis occurs in seminiferous tubules.
- Matured spermatozoa are released from Sertoli cells.
- Sperms are stored, matured & gains motility in epididimis.
- Capacitation occurs in female genital tract.

Testicular functions:

Seminiferous tubules	Interstitial cells of Leydig
Primitive germ cells: ○ Mature into spermatocytes Sertoli cells: ○ *Secrete: • -Inhibin & Activin • Androgen binding Protein • -Mullerian Inhibiting Substance(MIS) ○ *Acts as Blood Testes barrier	○ Secrete testosterone

- Erection- Mediated by para-sympathetic fibres.
- Ejaculation- Mediated by sympathetic fibres.

DMA'S CORNER OF WISDOM

SEMEN			
Characters	Seminal vesicle secretions	Prostatic secretions	Motility
*2—4 ml/ejaculate *100 million sperms/ml. * contains hyaluronidase	*60% of total volume * Fructose, Choline, Prostaglandins	*20% of total volume *Spermine, Fibrinolysin, Zinc, Acid phosphatase	-App. 3mm/min -Reaches the tubes within 30-60 mins of copulation

○ Erection	-dilatation of blood vessels in the erectile tissue of penis -Para sympathetic response, mediators are NO, VIP
○ Emission	-movement of semen to the ejaculatory ducts -sympathetic response
○ Ejaculation proper	-Rhythmic contraction of the penile musculature to exit the sperm -mediated by somatic afferents

- EJACULATION= Emission + Ejaculation proper
- Both sympathetic & somatic fibres have their roles; Emission is most prior than ejaculation, hence the major action is mediated via sympathetic fibres

FEMALE REPRODUCTIVE SYSTEM:

- Order of puberty: Thelarche → Pubarche → Menarche [TPM]

Ovarian cycle:

- Follicular enlargement → **dominant follicle(6th day)** → **secrete oestrogen** → graafian follicle → maturation of ovum → follicular rupture & release of ovum into the peritoneal cavity(ovulation) → remnants of graafian follicle forms **corpus luteum** → **secretes progesterone > oestrogen** → lysis of corpus luteum 2 days before menstruation leaving a fibrous scar called corpus albicans.

Hormonal influence:

- FSH-early development of G. Follicle.
- Final maturation of ovum- FSH & LH
- LH- ovulation, formation & maintenance of C Luteum.

Menstrual cycle:

Phase	Other names	Period	Endometrial changes
Proliferative phase (oestrogen)	• Preovulatory/ Post menstrual/Follicular phase	• 6 th day - 14 th day.	✓ *endometrial glands enlarge & proliferates ✓ *Increased vascularity & coiled arteries ✓ * Thickness: 2-3 mm
Secretory phase (progesterone)	• Post ovulatory/ premenstrual/ luteal/progestational phase	• 15 th day- 27 th day	✓ *endometrial glands hypertrophies & distended with mucus. ✓ *Increase in no. of coiled arteries, increased blood flow ✓ * Thickness: 5-6 mm
Menstrual phase	• Destructive phase/ bleeding phase		✓ Vasoconstriction of spiral arteries → ischemic changes → necrosis of endometrium → shedding. ✓ Bleeding: 75% arterial .

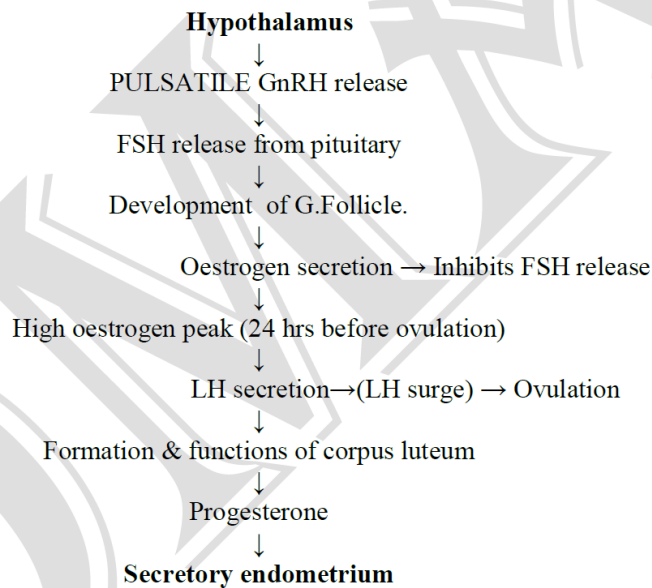
OVARIAN HORMONES:

DMA: 291/139, 3rd floor, Thambu Chetty ST, Parrys, Chennai -01
Phone number: 044-42009468 **Mail us:** studyatdma@gmail.com
Web: www.dma-study.com & www.jzmustudy.com

DMA'S CORNER OF WISDOM

Oestrogen	Progesterone	Inhibin	Relaxin	Activin
• Oestrone: more in post menopause • -Oestradiol: Most potent • -Oestriol: least potent, ↑ed during pregnancy • Synthesised by Theca interna, granulosa cells, corpus luteum. 97% protein bound, $T_{1/2}$-4 mins • *Other actions: ✓ Development of female secondary sexual characters ✓ Fat deposition & -↓ cholesterol ✓ -↑ osteoblastic activity ✓ - ↑ the number of Oxytocin receptors & their sensitivity in late pregnancy.	• Synthesised in Corpus luteum. • *97% protein bound, $T_{1/2}$-2 mins • Suppresses ovulation & menstruation in pregnancy. • - Thermo genic effect	• *Secreted by sertoli cells in males & granulosa cells in females. • *Inhibits FSH secretion	• Secreted by corpus luteum & placenta • *Relaxes the pelvis during pregnancy & helps in cervical ripening.	• *Secreted by sertoli cells in males & granulosa cells in females. • *Stimulates FSH secretion

Hormonal influence:



- **Oestrogens in small amount inhibit LH secretion whereas it stimulates LH release in higher concentrations.**

ESTROUS CYCLE:

- Mammals other than primates do not menstruate & their sexual cycle is called an estrous cycle.
- No episodic vaginal bleeding occurs but the underlying endocrinal mechanisms are essentially the same as those in the menstrual cycle.
- In other species ovulation is induced by copulation.(reflex ovulation)

FETUS:

- **Volume of blood in new born – 285 ml.**
- **Feto-placental unit:** Placenta lacks certain enzymes for steroid genesis. The intermediate products enter the fetal circulation & forms steroid in fetal liver & adrenals and transferred back to placenta. Thus the fetus & placenta functions as a single unit called **Feto-placental unit**.
- **Placenta** - Site for gaseous exchange in fetal life.

DMA'S CORNER OF WISDOM

- Human Chorionic Somatotropin / human Placental Lactogen /Chorionic Growth hormone Prolactin- **Maternal Growth Hormone of pregnancy**
- **In Vitro fertilization:**
 - Administration of ovulation inducing agent → Oocytes are recovered from developed G. Follicle by laparoscopy → Fertilized & Incubated → embryo reaches 4-8 cell stage → Embryo placed in the uterine cavity.
 - Success rate: 20%

LACTATION

- Oestrogen- Proliferation of mammary ducts.
- Progesterone- Lobulo-alveolar development.
- Prolactin- Initiation of milk secretion & maintenance.
- Oxytocin - Milk ejection.
- Mammogenesis: Development of the breast.
- Lactogenesis: Initiation of milk secretion
- Galactopoiesis: Maintenance of milk secretion
- **Chiari-Frommel syndrome:** Persistence of lactation & amenorrhea in women who do not nurse after delivery. Due to persistent prolactin secretion without FSH & LH.

Physiological causes of Gynecomastia:

- An
- drogen resistance
- Oestrogen therapy & Oestrogen secreting tumors
- Hyperthyroidism, Cirrhosis
- Drug induced
- ↑ plasma oestrogen/androgen ratio due to either increased circulating estrogens or decreased circulating androgens,

HYPOTHALAMUS

Regulation	Part of hypothalamus
○ Increased ECF osmolarity	○ Osmoreceptors-Anterior hypothalamus
○ Response to heat	○ Anterior hypothalamus
○ Response to cold	○ Posterior hypothalamus
○ Emotion	○ Dorsal and posterior hypothalamus
○ Circadian rhythm	○ Suprachiasmatic nucleus
○ GnRH secretion	○ Arcuate nucleus
○ TSH [via TRH secretion]	○ Paraventricular & neighbouring nuclei
○ Prolactin via PRH & PIH	○ Arcuate nucleus
○ Oxytocin release	○ Paraventricular nucleus(mainly)
○ ADH release	○ Supra optic nucleus(mainly)
○ Satiety centre	○ Ventro medial nucleus
○ Feeding centre	○ Lateral nucleus

DMA'S CORNER OF WISDOM

EXCRETORY SYSTEM

NEPHRONS:

- 1 to 1.3 millions in number per kidney.
- Length of each nephron: 45-65mm.

JG Apparatus: Consists of

- **Macula densa**- DCT comes closer to its own glomerulus & their cells at this site become columnar and are closely crowded together to form macula densa.
- **Lacis cells**- agranular cells situated between afferent & efferent arteriole.
- **Juxta glomerular (JG) cells**- epithelial cells in the tunica media of afferent arterioles. Secrete Renin.

Collecting tubules:

- **P cells**: principal cells increase the permeability of CT to water under the influence of ADH, via Aquaporin-2.
- **I cells**: Intercalated cells- secretes acid.
- **Note**: aquaporin 1 is present in the PCT.

Differentiating features between the two major types of nephrons

Feature	Cortical nephron	Juxta- medullary nephron
Occupancy	• 85%	• 14-15%
Glomerular size	• Smaller	• Larger
Henle's loop	• Shorter	• Longer
Features of HL	• Thin DHL, thick AHL	• Thin DHL, thin AHL, thick AHL
Vascular supply	• Peri tubular capillaries	• Vasa recta
Filtration rate	• Slow	• High
Function	• Excretion of waste products	• Concentration of urine

Peculiarities of renal circulation:

- Renal blood flow (RBF)- 1.2L/min.
- Renal plasma flow (RPF)- 700ml/day.
- GFR- 125ml/min or 180L/ day.
- Renal blood flow per gram tissue: 300-400 ml/ 100g/min [**maximum**]
- A-V O₂ difference across kidneys is very low. Renal venous blood has high PO₂ content- saturated with > 80% of O₂.
- O₂ consumption by the kidneys (VO₂) : 18-20 ml/min
- Renal blood flow & VO₂ : maximum in the cortex than the medulla.
- Auto regulation occurs only via the cortical blood flow. It fails if the perfusion pressure falls below 50mmHg.

Region	Blood Flow		O ₂ Consumption		Percentage of total	
	ml/min	ml/100g/min	ml/min	ml/100g/min	Cardiac output	Oxygen Consumption
LIVER	1500	57.7	51	2.0	27.8	20.4
KIDNEYS	1260	420	18	6.0	23.3	7.2
BRAIN	750	54	46	3.3	13.9	18.4
SKIN	462	12.8	12	0.3	8.6	4.8
SKELETAL MUSCLE	840	2.7	50	0.2	15.6	20.0
CARDIAC MUSCLE	250	84	29	9.7	4.7	11.6
WHOLE BODY	5400	8.6	250	0.4	100	100

DMA'S CORNER OF WISDOM

Glomerular filtration

- First step in urine formation.
- Depends on Starling's forces.
- **GFR increased in:** increased RBF & hypo proteinemia.
- **GFR decreased in:** old age, dehydration, ureteric obstruction & hydronephrosis.
- Filtration barriers: (**glomerular capillary wall- filtering membrane**). Consists of
 - Fenestrated endothelial cells
 - Glomerular basement membrane (**Type-IV collagen**)
 - Visceral epithelial cells (**Podocytes**)
- **Mesangial cells:**
 - Supporting unit for the glomerulus, mesenchymal in origin.
 - Proliferative, contractile and phagocytic.
 - Secrete matrix.

Agents causing contraction/ relaxation of Mesangial cells

- **Mesangial contraction** → decreases GFR
- **Mesangial relaxation** → increases GFR

Mesangial contraction	Mesangial relaxation
○ Angiotensin – II, Endothelin ○ ADH, Histamine ○ Leukotriene- C & D ○ Nor epinephrine ○ PAF, PDGF ○ PGF₂, Tx A₂	○ cAMP ○ ANP ○ PGE₂ ○ dopamine

- **Filtration fraction:** $GFR / RPF = 125/700 = 16-20\%$ of RPF
- **Filtered load:** amount of substance transported across the glomerular membrane per unit time. (Mg/min)

$GFR \times \text{Plasma concentration of the solute.}$

If excretion rate exceeds GFR → secretion has occurred.

If excretion less than GFR → reabsorption has occurred.

TRANSPORT OF INDIVIDUAL SUBSTANCES

- **Renal tubular transport maximum [T_m]:** maximal amount of a given solute that can be transported (secreted/ reabsorbed) renal tubules across / min.
 - i. Highest attainable rate of reabsorption - maximal tubular reabsorptive capacity (T_m / T_R)
Substances are: phosphate, sulphate, glucose, uric acid & albumin
 - ii. Highest attainable rate of Secretion - maximal tubular secretory capacity (T_m / T_s)
Substances are: Penicillin, diuretic, Vit-B, PAH, Salicylate.
- **Exception: uric acid & K^+ (only plasma electrolyte) can be both reabsorbed and secreted.**
 - PCT: reabsorbs 65 % OF Na^+ , Cl^- , HCO_3^- & water.
 - 100% of K^+ , HPO_4^- , amino acids & glucose.
 - Glucose: appears in urine when renal threshold is exceeded i.e., at 200 mg glucose / 100ml of arterial plasma. Or at 180 mg glucose / 100ml of venous plasma.
 - T_{MG} : 375 mg/min

Water reabsorption:

- **60-70 %: occurs in PCT**
- 5-10% in HL
- 5-8 %: in early part of DCT.
- **10-12 % in late part of DCT & Collecting ducts [ADH mediated]**
- **Obligatory water reabsorption:** In the PCT, passive reabsorption of water occurs secondary to the active reabsorption of Na^+ .
- **Facultative water reabsorption:** ADH mediated water reabsorption in the late part of DCT & Collecting ducts.
- **Thus in the absence of ADH 12% of water is excreted increasing the urine flow to 20L/day.**

DMA'S CORNER OF WISDOM

24 HOURS RENAL HANDLING OF VARIOUS SUBSTANCES					
Substance	Filtered	Reabsorbed	Secreted	Excreted	Percentage Reabsorbed
Sodium(mEq)	26,000	25,850		150	99.4
Potassium(mEq)	600	560	502	90	93.3
Chloride(mEq)	18,000	17,850		150	99.2
Bicarbonate(mEq)	4900	4900		0	100
Urea(mmol)	870	460		410	53
Creatinine (mmol)	12	1	1	12	
Uric Acid(mmol)	50	49	4	5	98
Glucose (mmol)	800	800		0	100
Water(ml)	1,80,000	1,79,000		1000	99.4

Hormones and their site of action

Hormones	Site
○ Angiotensin-II	○ Constricts afferent arterioles, reduces GFR
○ Aldosterone	○ Cortical collecting ducts.
○ ADH	○ Late DCT & medullary CD
○ ANP	○ Collecting ducts

TUBULO GLOMERULAR FEEDBACK

- Auto regulation of the kidneys that link changes in NaCl concentration at the macula densa (**tubular component**) with the control of arteriolar resistance (**glomerular component**).
- Sensor: macula densa.

RENAL FUNCTION TESTS

- Clearance : (ml/min) = Amount of substance excreted/ min / plasma concentration of the substance = $U_s \times V / P_s$
- GFR → measured by measuring the excretions and plasma level of a substance that is freely filtered through the glomeruli but neither secreted nor reabsorbed by the tubules.
- **Criteria of an ideal substance to measure GFR:**
 - Should be filtered freely.
 - Not reabsorbed/ secreted
 - Not metabolized
 - Not stored in the kidney
 - Non toxic.
- Ideal substance: **Inulin** (practical purpose: **creatinine**)
- Normal range of creatinine clearance: 80- 110ml/min
- **PAH & diodrast measures: renal blood flow.**

CONCENTRATION OF URINE [counter- current system]

- During over hydration - diluted urine is excreted → upto a level of 50mOsm/kg i.e., 1/6th of plasma osmolality.
- During dehydration - Conc. urine is excreted → upto a level of 1200mOsm/kg i.e., 4 times plasma osmolality.
- **This is achieved by counter current system, a feature of Juxta-medullary nephrons.** It consists of DLH, ALH, medullary interstitium, DCT, CD and Vasa recta.
- Concentrating mechanism- depends on the existing of a gradient of increasing osmolality towards the interior of medullary pyramids. This gradient is:
 - Produced by → Henle's loop & collecting ducts [**counter current multiplier**]
 - Maintained by → Vasa Recta [**counter current exchanger**]
 Urea plays a major role in maintaining the CCS.

Other sites of counter current mechanism:

- Venae comitantes of limbs (artery → vein), helps in heat dissipation.
- Blood vessels of the villi in the small intestine.

DMA: 291/139, 3rd floor, Thambu Chetty ST, Parrys, Chennai -01
Phone number: 044-42009468 Mail us: studyatdma@gmail.com
Web: www.dma-study.com & www.jzmustudy.com

DMA'S CORNER OF WISDOM

- Testes

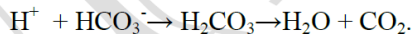
Specific functions at different sites of the nephron

- **GFR:** Isotonic to plasma.
- **PCT:** active absorption of solutes (65%), passive diffusion of water (65%)
 - Fluid in the PCT: **isotonic**
- **DHL:** permeable to water, impermeable to solutes (minimal permeability for urea)
 - Fluid In The DHL: **Hypertonic (concentrating segment)**
- **AHL (thin & thick ascending), early DCT:** impermeable to water, permeable to solutes
 - Fluid in the AHL & early DCT: **hypotonic (diluting segment)**
- **Late DCT & collecting tubules:** more permeable to water
 - Fluid reaching the collecting ducts: **Isotonic/ hypertonic.**
- Proximal tubule is the main site for reabsorption of water and electrolytes,.
- Glucose is almost completely reabsorbed, i.e. least clearance in urine. (Glucose & urea are 100% reabsorbed.).
- About 80-90% of filtered bicarbonate reabsorption occurs in the proximal tubule.
- About 50-60% of filtered water is reabsorbed in PCT obligatory to Na⁺ reabsorption.
- About 60% of filtered Na⁺ is reabsorbed in proximal tubules.
- Thin & thick ascending limb of LOH, early distal tubules are impermeable to water.
- >50% potassium that appears in urine is derived from secretion by distal tubule.
- Osmolality of urine depends on the action of vasopressin on collecting ducts.
- Acidification of tubular fluid (urine) occurs in collecting ducts.

ACIDIFICATION OF URINE

HCO₃⁻ REABSORPTION:

- occurs throughout the nephron except in DHL.
- 90% occurs in the PCT by secondary active transport via Na⁺ H⁺ exchanger.
- The secreted H⁺ reacts with the filtered HCO₃⁻ and forms H₂CO₃.
- The brush borders of the PCT contain carbonic anhydrase. It catalyzes the rapid dehydration of H₂CO₃ to form H₂O & CO₂.



H⁺ SECRETION:

- Occurs in hand with HCO₃⁻ reabsorption.
- for one mole of H⁺ secreted, one mole of Na⁺ & one mole of HCO₃⁻ are reabsorbed.
 - 85% secretion → from PCT
 - 10% → DCT
 - 5% → collecting tubules.

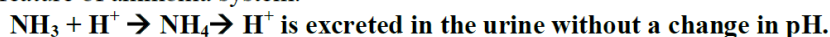
Buffer system in the kidneys

i. Bicarbonate system

ii. Phosphate system

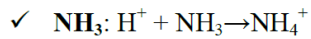
iii. Ammonia system: synthesised in the DCT & CT, not filtered.

- Characteristic feature of ammonia system:



- The maximal H⁺ gradient against which the transport mechanisms can secrete acid corresponds to a urine pH of about 4.5(**the limiting pH**). It is normally reached in the collecting ducts.
- If there were no buffers, this pH would be reached rapidly and H⁺ secretion would stop.
- However the three important buffers remove free H⁺ permitting more acid to be secreted.
- They are:
 - ✓ **HCO₃⁻:** $\text{H}^+ + \text{HCO}_3^- \rightarrow \text{H}_2\text{O} + \text{CO}_2$
 - ✓ **HPO₄²⁻:** $\text{H}^+ + \text{HPO}_4^{2-} \rightarrow \text{H}_2\text{PO}_4$

DMA'S CORNER OF WISDOM



Body buffer systems:

- A. Hemoglobin system: mainly due to the presence of imidazole groups of the histidine residues. As it is present in larger quantities, the **buffering capacity is 6 times more than that of plasma proteins.**
- B. Protein system
- C. Carbonic acid- bicarbonate system
- D. Phosphate system

Characteristics of Primary Acid-Base Disturbances

	pH	H ⁺	Pco ₂	HCO ₃ ⁻
Normal	7.4	40 mEq/L	40 mm Hg	24 mEq/L
Respiratory acidosis	↓	↑	↑↑	↑
Respiratory alkalosis	↑	↓	↓↓	↓
Metabolic acidosis	↓	↑	↓	↓↓
Metabolic alkalosis	↑	↓	↑	↑↑

ANION GAP

- Difference between the concentration of cations (other than Na) and anions (other than Cl & HCO₃).
- Includes proteins, sulfates, phosphate ions, organic acids.

High anion gap metabolic acidosis	Non anion gap metabolic acidosis
1. Lactic acidosis: Shock, Cardiac failure, Acute respiratory failure, Metformin therapy. 2. Ketoacidosis: DKA, Alcoholic, Starvation. 3. Ingested toxins: Ethylene glycol, Methanol, Salicylates 4. ARF & CRF	1. Gastro intestinal bicarb loss: Diarrhea, uretero sigmoidostomy, external pancreatic drainage, drugs like MgSo ₄ , CaCl ₂ , Cholestyramine 2. Renal tubular acidosis 3. Ingestion of ammonium chloride 4. Carbonic Anhydrase inhibitors like acetazolamide

Factors that affect Renin Secretion

STIMULATORY	INHIBITORY
○ *Increased sympathetic activity & circulatory catecholamines ○ *Prostaglandins, Diuretics, dehydration, hypotension ○ *Decreased sodium in DCT, Cirrhosis, cardiac failure, hemorrhage ○ *Upright posture ○ *Constriction of renal artery or aorta	○ *High Na⁺ Concentration in DCT ○ *Increased Na⁺ & Cl⁻ reabsorption across macula densa ○ *Increased afferent arteriolar Pressure ○ *Vasopressin & Angiotensin - II

PHYSIOLOGY OF MICTURITION

Nerve supply of bladder:

1. Afferent:

- i. From external sphincter and posterior urethra → pudendal nerve → dorsal nerve roots of S2, 3, 4.
- ii. From the body, trigone & internal sphincter, afferent fibres take a double route.
 - a. Along the sympathetic nerve → dorsal nerve roots of L1,2 and lower thoracic segments.
 - b. Along the sacral parasympathetic nerves → sacral dorsal nerve roots.

2. Efferent:

Type	Origin	Course	Pars innervated	Effect of stimulation
Sympathetic	• L 1, L2 segments of spinal cord	• Lateral sympathetic chain → celiac & superior mesenteric ganglia → pre sacral	• Body • Trigone • Internal	• *relaxation of detrusor • *contraction of trigone & internal

DMA: 291/139, 3rd floor, Thambu Chetty ST, Parrys, Chennai -01

Phone number: 044-42009468 Mail us: studyatdma@gmail.com

Web: www.dma-study.com & www.jzmustudy.com

DMA'S CORNER OF WISDOM

		nerve --> 2 hypogastric nerves --> hypogastric ganglia --> bladder	sphincter	sphincter → urine retention
Para sympathetic	Pre ganglionic cells from S2,3,4 segments of S.C	Nervi erigentes (pelvic nerves)--> hypogastric ganglia--> post ganglionic fibres--> bladder	- Body - Trigone - Internal sphincter	*contraction of detrusor * relaxation of trigone & internal sphincter → bladder emptying
Somatic	Anterior horn cells of S2,3,4	Pudendal nerve	External sphincter prostatic urethra	Higher control, voluntary micturition.

- SENSATION OF STRETCH → SACRAL PARA SYMPATHETICS
- SENSATION OF PAIN → SYMPATHETIC NERVE.

MICTURITION REFLEX:

- **Afferent:** dorsal nerve root S2, S3, S4 via pelvic nerves.
- **Efferent:** dorsal nerve root S2, S3, S4 via para sympathetic nerves.
- **Centre:** Spinal Cord

Control of micturition by higher centers:

- **Cortical center:** can inhibit or initiate micturition even if there is no desire to void urine.
- **Facilitatory center: Pons & posterior hypothalamus.** It exerts a facilitatory effect on the spinal micturition center.
- **Inhibitory center: Midbrain.** It inhibits spinal centers at the unconscious level.

CYSTOMETROGRAM:

- Shows 3 components:
 - Initial slight rise in pressure, upto 10 cm H₂O when the first increment in volume, upto 100ml is produced.
 - A long nearly flat segment is seen with further increment upto 300-400ml. this is due to the intrinsic tone of the bladder wall itself.
Laplace law: Tension (T) in the wall of a cylinder is equal to the product of the transmural pressure (P) and the radius of the tube (r) divided by the wall thickness.
 - Further collection of urine results in a sudden sharp rise in pressure as the micturition reflex is triggered.
 - First urge to void -about 150ml. Volume that initiates a reflex contraction is 300-400ml.
 - Sympathetic nerves play no part in micturition, but they mediate the contraction of the bladder muscle that prevents semen from entering the bladder during ejaculation.
 - Voluntary contraction can be done by facilitation of the spinal voiding reflex when it contains only a few ml of urine.

ABNORMALITIES OF BLADDER FUNCTION

a. Sensory denervated bladder (Atonic bladder):

- Occurs due to lesions of sacral posterior nerve roots.
- Stretch impulses are not transmitted to the center, leading to over distension and overflow dribbling.
- Bladder is thin walled, flaccid, distended & hypotonic.

b. Denervated bladder (Autonomous bladder):

- Both afferent & efferent fibers are interrupted & the bladder is isolated from the spinal cord.
- Initially the bladder is flaccid & distended. Later becomes active and partially expel its contents.
- Bladder gets shrunken & atrophies.
- E.g. Cauda equina lesion or section of pelvic nerves.

DMA: 291/139, 3rd floor, Thambu Chetty ST, Parrys, Chennai -01
Phone number: 044-42009468 **Mail us:** studyatdma@gmail.com
Web: www.dma-study.com & www.jzmustudy.com

DMA'S CORNER OF WISDOM

c. **Acute complete transection of spinal cord above sacral segments:**

- Stage-I (Spinal shock): Retention of urine.
- Stage-II (Reflex activity): reflex micturition with no voluntary control. (**Automatic bladder**).
- Stage-III (failure of reflex activity): Urinary incontinence.

d. **Uninhibited neurogenic bladder:**

- a. Occurs in lesions in which the cortico-spinal inhibitory fibres are damaged, leaving the facilitatory fibres intact.
- b. There is increased frequency with voiding of small quantities.

e. **Nocturnal enuresis:**

- Physiological- in children.
- Pathological-in Lumbo-sacral vertebral defects

- **Obligatory Volume:** Minimum amount of urine necessary to remove all waste products, with a normal diet, called Obligatory Volume is 500ml/day.
- **Oliguria:** less than 500ml/day
- **Anuria:** less than 50ml/day
- **Mechanism of heat loss from the body:**
 1. Radiation – 50%
 2. conduction & convection -20%
 3. vaporization of sweat & insensible water losses- 27%
 4. warming & humidification of air- 2%
 5. excretion in urine & faeces- 1%

DMA WEB APP FOR FMGE/NEXT (INDIA)

Free version of web-app with 25,000 MCQs divided in chapter wise , subject wise & mock fashion+ limited image based MCQs + revision materials + Insight to FMGE with study plans & tips.

How to register for the free version?

- **Step 1:** www.dma.testpress.in
- **Step 2:** Add username, password & mail ID
- **Step 3:** You can choose only one exam to acquire free access
- **Step 4:** Activate the link sent to your mail (**Check inbox & spam**)
→ **You will be approved in 1 day**
- **Download app:** <https://play.google.com/store/apps/details?id=in.testpress.dma>



+8615941687327
+8615841616754
+8618841649297



Mail us: studyatdma@gmail.com
Web: www.dma-study.com



DAVINCI
MEDICAL
ACADEMY



锦州医科大学

Sponsored:

SALIENT FEATURES

INSIGHT

TIPS

TESTS

NEWS

MATERIALS



DMA CLASS





DAVINCI MEDICAL ACADEMY

India Helpline : +91-9884329457 | +91-9962850383 | +91 8680026100

For Enrolment and Enquiry: +91 9884393008 | +91 87544 17895

China Helpline :+8615940651819

Chennai: F-161, 1st Floor, 3rd Phase, #768, Spencer Plaze, Anna Salai, Chennai - 600 002

Headoffice: No: 291/139, Illrd Floor, Thambu Chetty Street, Parrys, Chennai-600001, Tamilnadu, India.

www.dma-study.com | studyatdma@gmail.com